In re Application of: Dror OFER
Serial No.: 10/523,131
Filed: January 21, 2005
Office Action Mailing Date: June 3, 2008

Examiner: Michael L. BORIN
Group Art Unit: 1631
Attorney Docket: 35898

**In the Claims:**

1. (Currently Amended) A method of obtaining information about a chemically active area of a target molecule, comprising:

providing a set of compounds comprising a set of substantially rigid chemical gauges, each of said gauges comprising at least one set of three binding points in a substantially rigid triangular configuration;

for each of said gauges, defining at least one ~~providing at least one substantially rigid~~ triangular geometric substructure which represents a set of three binding points, each triangular geometric substructure being defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices;

performing a plurality of assays for measuring an interaction of said target with said gauges, each assay measuring an interaction of said target with at least one of said gauges, thereby obtaining a plurality of assay results; and

analyzing said assay results using a plurality of said triangular geometric substructures to obtain information about said chemically active area,

said set of gauges being selected such that at least 50% of a ~~mathematical chemical~~triangle space is spanned by ~~the substantially rigid triangular geometric substructures of~~ said gauges,

said triangle space defining all possible 3-point pharmacophores defined by a triplet of distances that form a triangle, each distance being in a range of 2-12 angstrom, and by a triplet of chemical binding point types for the triangle vertices, each chemical binding point type being selected from the group consisting of ~~, each point in said space being covered by at least 5 distinct gauges from said set;~~

~~said mathematical chemical space being defined using a list of at least six chemical binding point types, including~~ acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic, wherein said 3-point pharmacophore represents a set of three binding points on a molecule to which a gauge may bind ~~and a range of possible distances between chemical binding points including the range of~~

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~~2-12 angstrom, said list and said range defining a space of possible triangular configurations, each configuration including a triplet of distances within said range that form a triangle and a triplet of binding types for the triangle vertices~~; and

a portion of said space being defined as being spanned if there are~~is~~ at least six ~~one substantially rigid triangular substructure available~~gauges with a substantially rigid triangular configuration of binding points capable of ~~to~~ chemically binding to each 3-point pharmacophore defined by~~a triangular configuration of binding points selected in~~ said portion of said space.~~,~~

~~causing said target to interact with a plurality of gauges of said set of gauges;~~

~~assaying said interaction of said gauges with said target to obtain a plurality of assay results; and~~

~~analyzing said assay results to obtain information about said chemically active area.~~

2. (Currently Amended) A method according to claim 1, wherein said set of gauges is selected such that at least 50% of~~space includes~~ a portion of said triangle space covering the range of distances of between 4 and 8 angstrom~~, said portion~~ is spanned ~~at least 50%~~.

3. (Original) A method according to claim 1, wherein said gauges are constructed using a rigid scaffold.

4. (Original) A method according to claim 1, wherein constituent atoms of said gauges do not move more than 1 Å unless at least 20Kcal/Mol are applied to the gauge.

5. (Original) A method according to claim 1, wherein analyzing comprises identifying a plurality of spatial and chemically specific bindings configurations in said target active area.

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6. (Currently Amended) A method according to claim 5, wherein said configurations comprise 3-point pharmacophores~~triangular configurations~~.

7. (Withdrawn-Currently Amended) A method according to claim 5, wherein identifying comprises identifying a 3-point pharmacophore~~configuration~~ that matches a triangular configuration of a bound gauge.

8. (Currently Amended) A method according to claim 5, wherein identifying comprises identifying a 3-point pharmacophore~~configuration~~ that does not match a triangular configuration of a bound gauge.

9. (Original) A method according to claim 8, wherein identifying comprises identifying by statistical analysis of said assay results.

10. (Withdrawn) A method according to claim 9, wherein identifying comprises identifying by clustering.

11. (Withdrawn) A method according to claim 5, wherein identifying comprises assuming each gauge indicates a single configuration.

12. (Withdrawn) A method according to claim 5, wherein identifying comprises assuming at least some of the gauges indicate a plurality of configurations.

13. (Withdrawn) A method according to claim 5, wherein identifying comprises classifying gauges by chemical moieties at vertexes of said configurations.

14. (Currently Amended) A method according to claim 1, comprising reconstructing a spatial map of at least part of said chemically active area, from at

least two of said assay results, said spatial mappart including at least four chemical binding areas.

15. (Currently Amended) A method according to claim 14, wherein said spatial mappart includes at least six chemical binding areas.

16. (Withdrawn-Currently Amended) A method according to claim 5, comprising reconstructing a spatial map of at least part of said chemically active area, from at least two of said configurations, said spatial mappart including at least four chemical binding points.

17. (Withdrawn-Currently Amended) A method according to claim 16, wherein said spatial mappart includes at least six chemical binding areas.

18. (Withdrawn) A method according to claim 16, wherein reconstructing comprises:

test-reconstructing a plurality of spatial maps from said configurations;
scoring said maps; and
selected a spatial map based on its score.

19. (Withdrawn) A method according to claim 16, wherein reconstructing comprises:

test-reconstructing a plurality of spatial maps from said configurations;
clustering said maps according to common substructures; and
selected a spatial map based on a relative property of a cluster it belongs to.

20. (Withdrawn) A method according to claim 19, wherein said relative property comprises size.

21. (Original) A method according to claim 16, wherein said spatial map includes enough binding points to ensure binding of a small molecule drug having a chemical profile matching the binding points.

22. (Withdrawn) A method according to claim 21, wherein said spatial map includes at least 6 binding points.

23. (Withdrawn) A method according to claim 21, wherein said spatial map includes at least 8 binding points.

24. (Currently Amended) A method according to claim 1, wherein said set of gauges comprises a set of gauges with at least 10,000 distinct gauges.

25. (Currently Amended) A method according to claim 1, wherein said set of gauges comprises a set of gauges with at least 50,000 distinct gauges.

26-28. (Canceled)

29. (Currently Amended) A method according to claim 1, wherein at least 0.5% of said gauges bind with said target when said target is interacted with said gauges.

30. (Currently Amended) A method according to claim 1, wherein at least 1% of said gauges bind with said target when said target is interacted with said gauges.

31. (Currently Amended) A method according to claim 1, wherein at least 3% of said gauges bind with said target when said target is interacted with said gauges.

32. (Original) A method according to claim 1, wherein at least 50% of said gauges are defined by adding moieties to a set of fewer than 100 scaffolds.

33. (Original) A method according to claim 1, wherein at least 50% of said gauges are defined by adding moieties to a set of fewer than 50 scaffolds.

34. (Currently Amended) A method according to claim 1, wherein ~~at least~~ said set of gauges uses fewer than 15 different chemical moieties to define the chemical behavior of said gauges.

35. (Currently Amended) A method according to claim 1, wherein ~~at least~~ said set of gauges uses fewer than 10 different chemical moieties to define the chemical behavior of said gauges.

36. (Original) A method according to claim 1, wherein said assay is a functional assay.

37. (Withdrawn) A method according to claim 1, wherein said assay is a binding assay.

38. (Withdrawn) A method according to claim 1, wherein said assay is a cellular assay.

39. (Withdrawn) A method according to claim 1, wherein said assay is a flow-through assay.

40. (Original) A method according to claim 36, wherein said functional assay is performed in the presence of a natural substrate of said target.

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41. (Original) A method according to claim 1, wherein said target comprises a protein including a biochemically active area adapted to engage a substrate.

42. (Original) A method according to claim 41, wherein said chemically active area comprises an area including said biochemically active area.

43. (Original) A method according to claim 41, wherein said chemically active area comprises a control area of said protein.

44. (Currently Amended) A method according to claim 1, wherein said analyzing comprises analyzing successful binding of at least 60 distinct gauges.

45. (Currently Amended) A method according to claim 1, wherein said analyzing comprises analyzing successful binding of at least 10 distinct gauges.

46. (Currently Amended) A method according to claim 1, wherein said analyzing comprises analyzing successful binding of at least 100 distinct gauges.

47. (Original) A method according to claim 5, wherein identifying comprises identifying at least 40 different configurations.

48. (Original) A method according to claim 5, wherein identifying comprises identifying at least 10 different configurations.

49. (Original) A method according to claim 5, wherein identifying comprises identifying at least 100 different configurations.

50. (Withdrawn) A method according to claim 16, comprising:

comparing said map to a lead data base; and

selecting a lead from said data base for further use responsive to a semblance or lack of semblance between said lead and said map.

51. (Withdrawn) A method according to claim 16, comprising:

comparing said map to a lead data base; and

rejecting a lead from said data base for further use responsive to a semblance between said lead and said map.

52. (Withdrawn) A method according to claim 16, comprising:

constructing a lead to have a semblance to said map.

53. (Withdrawn) A method according to claim 52, wherein constructing comprises constructing using said gauges or scaffolds used to define said gauges.

54. (Original) A method according to claim 5, comprising:

comparing said configurations to a lead data base; and

selecting a lead from said data base for further use responsive to a matching of said configurations to said lead.

55. (Original) A method according to claim 5, comprising:

constructing a lead based on said configurations.

56. (Original) A method according to claim 5, comprising:

selecting at least one of said gauges as a lead for drug discovery.

57. (Withdrawn) A method according to claim 1, comprising comparing the binding of gauges with similar binding geometries to obtain steric clashing data; and

analyzing said steric clashing data to provide geometrical information about said target.

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58–101. (Cancelled)

102. (Withdrawn) A method according to claim 1, comprising generating a set of drug leads for said target based on said information.

103. (Withdrawn) A method according to claim 102, comprising removing known drug leads for said target from said set.

104–154. (Cancelled)

155. (Previously Presented) A method according to claim 1, wherein said analyzing comprises characterizing said chemically active area.

156. (Previously Presented) A method according to claim 155, wherein said chemically active area comprises at least two disjoint chemically active areas.

157. (Withdrawn) A method according to claim 1, wherein said analyzing comprises taking said rigidity into account of said analyzing.

158. (Previously Presented) A method according to claim 1, wherein said target molecule comprises an agricultural chemical target.

159. (Previously Presented) A method according to claim 1, wherein said target molecule comprise a drug target.

160. (Canceled)

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161. (Currently Amended) A method according to claim 1, wherein at least 0.1% of said gauges bind with said target when said target is interacted with said gauges.

162. (Currently Amended) A method according to claim 1, wherein said binding points of said gauges~~the moieties~~ comprise Hydroxyl (OH), Carboxyl (COOH), Amide (CONH2), Ethyl (CH2-CH3), Propyl (CH2-CH2-CH3), Phenyl (C6H5, 6 member aromatic ring).

163. (Previously Presented) A method according to claim 1, wherein said chemically active area comprises at least two disjoint chemically active areas.

164-171. (Cancelled)